

Amendments to the Specification

Please replace the paragraph beginning at page 10, line 15, with the following rewritten paragraph:

Figure 11 depicts the consensus sequence (SEQ ID NO:29) established from the DNA sequences of the four strains of *Neisseria* and indicates the substitutions or insertion of nucleotides specific to each strain.

Please replace the paragraph beginning at page 10, line 19, with the following rewritten paragraph:

Figure 12 depicts the consensus sequence (SEQ ID NO:30) established from the protein sequences of the four strains of *Neisseria* and indicates the substitutions or insertion of amino acid residues specific to each strain.

Please replace the paragraph beginning at page 11, line 8, with the following rewritten paragraph:

Figure 15 is a graphic representation of the synthetic peptides of the invention as well as their respective position in the full 22 kDa protein (SEQ ID NO:2) of *Neisseria meningitidis* strain 608B (B:2a:P1.2).

Please replace the paragraph beginning at page 31, line 1, with the following rewritten paragraph:

Interestingly, this study about the resistance of the 22 kDa protein to proteases indicated that another protein band with apparent molecular weight of 18kDa seems to be also resistant to enzymatic degradation (Figure 3a). Clues about this 18kDa protein band were obtained when the migration profiles on SDS-PAGE gels of affinity purified recombinant 22kDa protein were analyzed (Figure 3b). The 18 kDa band was apparent only when the affinity purified recombinant 22kDa protein was heated for an extended period of time in sample buffer

containing the detergent SDS before it was applied on the gel. N-terminal amino acid analysis using the Edman degradation (Example 3) clearly established that the amino acid residues (E-G-A-S-G-F-Y-V-Q) (SEQ ID NO: 31) identified on the 18 kDa band corresponded to the amino acids 1-9 (see SEQ ID NO:1). These results indicate that the 18 and 22kDa bands as seen on the SDS-PAGE is are in fact derived from the same protein. This last result also indicates that the leader sequence is cleaved from the mature 18 kDa protein. Further studies will be done to identify the molecular modifications explaining this shift in apparent molecular weight and to evaluate their impact on the antigenic and protective properties of the protein.

Please replace the paragraph beginning at page 41, line 26, with the following rewritten paragraph:

To confirm the correct expression of the cloned gene, the N-terminal amino acid sequence of the native 22 kDa surface protein derived from *Neisseria meningitidis* strain 608B was determined in order to compare it with the amino acid sequence deduced from the nucleotide sequencing data. Outer membrane preparation derived from *Neisseria meningitidis* strain 608B was resolved by electrophoresis on a 14% SDS-PAGE gel and transferred onto a polyvinylidene difluoride membrane (Millipore Products, Bedford Mass.) according to a previously described method [Sambrook et al., Molecular Cloning: a laboratory manual, Cold Spring Harbor Laboratory Press (1989)]. The 22 kDa protein band was excised from the gel and then subjected to Edman degradation using the Applied Biosystems Inc. (Foster City, CA) model 473A automated protein sequencer following the manufacturer's recommendations. The amino acid sequence E-G-A-S-G-F-Y-V-Q-A (SEQ ID NO: 32) corresponded to amino acids 1-10 (see SEQ ID NO:2) of the open reading frame, indicating that the *Neisseria meningitidis* strain 608B, 22 kDa surface protein has a 19 amino acid leader peptide (amino acid residues -19 to -1 of SEQ ID NO:2).

Please replace the paragraph beginning at page 54, line 14, with the following rewritten paragraph:

a) MCH88 strain: The nucleotide sequence of strain MCH88 (clinical isolate) is presented in Figure 8 (SEQ ID NO:3). From experimental evidence obtained from strain 608B (Example 3), a putative leader sequence was deduced corresponding to amino acid -19 to -1 (M-K-K-A-L-A-A-L-I-A-L-A-L-P-A-A-A-L-A) (SEQ ID NO: 33). A search of established databases confirmed that 22kDa surface protein from *Neisseria meningitidis* strain MCH 188 (SEQ ID NO:4) or its gene (SEQ ID NO:3) have not been described previously.

Please replace the paragraph beginning at page 54, line 24, with the following rewritten paragraph:

b) Z4063 strain: The nucleotide sequence of strain Z4063 (Wang J.-F. et al. Infect. Immun., 60, p.5267 (1992)) is presented in Figure 9 (SEQ ID NO:5). From experimental evidence obtained from strain 608B (Example 3), a putative leader sequence was deduced corresponding to amino acid -19 to -1 (M-K-K-A-L-A-T-L-I-A-L-A-L-P-A-A-A-L-A) (SEQ ID NO: 34). A search of established databases confirmed that 22kDa surface protein from *Neisseria meningitidis* strain Z4063 (SEQ ID NO:6) or its gene (SEQ ID NO:5) have not been described previously.

Please replace the paragraph beginning at page 55, line 1, with the following rewritten paragraph:

c) *Neisseria gonorrhoeae* strain b2: The nucleotide sequence of *Neisseria gonorrhoeae* strain b2 (serotype 1. Nat. Ref. Center for *Neisseria*, LCDC, Ottawa, Canada) is described in Figure 10 (SEQ ID NO:7). From experimental evidence obtained from strain 608B (Example 3), a putative leader sequence was deduced corresponding to amino acid -19 to -1 (M-K-K-A-L-A-A-L-I-A-L-A-L-P-A-A-A-L-A) (SEQ ID NO: 33). A search of established databases confirmed that 22kDa surface protein from *Neisseria gonorrhoeae* strain b2 (SEQ ID NO:8) or its gene (SEQ ID NO:7) have not been described previously.

Please replace the paragraph beginning at page 62, line 7, with the following rewritten paragraph:

A 540 nucleotide fragment was amplified by PCR from the *Neisseria meningitidis* strain 608B genomic DNA using the following two oligonucleotide primers (OCRR8: 5'-TAATAGATCTATGAAAAAAGCACTTGCCAC-3' and OCRR9: 3'-CACGCGCAGTTTAAGACTTCTAGATTA-5') (SEQ ID NOS: 27 & 28, respectively). These primers correspond to the nucleotide sequences found at both ends of the 22 kDa gene. To simplify the cloning of the PCR product, a Bgl II (AGATCT) restriction site was incorporated into the nucleotide sequence of these primers. The PCR product was purified on agarose gel before being digested with Bgl II. This Bgl II fragment of approximately 525 base pairs was then inserted into the Bgl II and Bam HI sites of the plasmid p629. The plasmid containing the PCR product insert named pNP2204 was used to transform *E. coli* strain DH5 α F'IQ. A partial map of the plasmid pNP2204 is presented in Figure 16. The resulting colonies were screened with *Neisseria meningitidis* 22 kDa surface-protein specific monoclonal antibodies described in Example 2. Western blot analysis of the resulting clones clearly indicated that the protein synthesized by *E. coli* was complete and migrated on SDS-PAGE gel like the native *Neisseria meningitidis* 22 kDa surface protein. Plasmid DNA was purified from the selected clone and then sequenced. The nucleotide sequence of the insert present in the plasmid perfectly matched the nucleotide sequence of the gene coding for the *Neisseria meningitidis* 22 kDa protein presented in Figure 1.

Please delete the section of the application entitled "Sequence Listing" on pages 69 - 84 and insert the enclosed Sequence Listing immediately after claim 207.